

FIG. 1

cvHAS	MG--KNIIIM	VSWYTIITS-	-----NL	IAVGGASLI	APAITGVLH	39
seHAS	MRTLKNLIT-	-----V	VAFSIFWVL	I-----VNV		25
spHAS	VPIFKKTLI-	-----V	LSFIFLISI	I-----LNM		25
huHAS	MHCERFLCIL	RI---IGTTL	-----FGVSL	LGITAAIVG		33
xlHAS	MK-EKAAETM	EIPEGIPKDL	EPKHPTLWRI	IYYSFGVVL	ATITAAVAE	49
cvHAS	WNIALST--I	WGVSATGIFV	FGFFLAQVLF	SELNRKRRLK	WISLRPKGWN	87
seHAS	YLFGAGK---	-SLSGVFL	IAYLLVKMSL	SFF-YKPFKG	R---AGQ--Y	65
spHAS	YLFGT-S---	-TVGIVGVIL	ITYLVIKLGL	SFL-YEPFKG	N---PHD--Y	64
huHAS	YQFIQTDNYY	FSFGLYGAF	ASHLIIQSFL	AFLEHRKMKK	SLETPIK--L	81
xlHAS	FQVLKHEAIL	FSLGLYGLAM	LLHLMQSLF	AFLEIRRVNK	S-ELPCS--F	96
cvHAS	DVRLAVITAG	YREDPYMFQK	CHESVRDSD	GNVA-RLICV	IDGDEDDDMR	130
seHAS	K--VAITIPS	YNEDAESLLE	TIKSVQQQT	PLAE--IYV	DDGSADETGI	111
spHAS	K--VAIVIPS	YNEDAESLLE	TIKSVLAQT	PLSE--IYI	DDGSNTDAI	110
huHAS	NKTVLCTAA	YQEDPDYLRK	CLQSVKRLT	PG--IKVVM	IDGNSEDDLY	129
xlHAS	KKTVALTITAG	YQENPEYLIK	CHESCKYVK	EKDKLKILV	IDGNTEDDAY	146
cvHAS	MAAVYKAIYN	DN-----	-----IKKPE	-----FV	LCESDDKEGE	165
seHAS	KR-----	---IEDYVRD	-----	TGDLSSNVV	HRSEKNQGR	140
spHAS	QL-----	---IEEVNR	-----	EVDICRNIV	HRSLVKNKGR	139
huHAS	MMDIFSEVMG	RDKSATYIWK	NNFHE-KGPG	ETDES-----	-----HKESS	168
xlHAS	MMEMFKDVFH	GEDVGTIVWK	GNVHTVKKPE	ETNKGSCPEV	SKPLNEDEGI	196
cvHAS	RIDSDF---S	RDICVLPHR	GKRECLYTG	QLAKMDPSVN	AVVLIDSDTV	212
seHAS	HA-----	---QAW-	-----A	E--RSDADV-	FLTVDSDY	163
spHAS	HA-----	---QAW-	-----A	E--RSDADV-	FLTVDSDY	162
huHAS	QHVTQLVLSN	KSICIMQKWG	GKREVMYTA	R--ALGRSDV	YVQVCDSDTM	216
xlHAS	NMVEELVRNK	RCVCIMQW	GKREVMYTA	Q--AIGTSVD	YVQVCDSDTK	244
cvHAS	LEKDAILEVV	YPLACDPEIQ	AVAGECKIWN	T-DTLLSLLV	AWRYSAECV	261
seHAS	IYPDALEELL	KTFNDPTVFA	ATG-HLNVNR	RQTNLTLRLT	DIRYDNEAGV	212
spHAS	IYPNALEELL	KSFNDETVYA	ATG-HLNVNR	RQTNLTLRLT	DIRYDNEAGV	211
huHAS	LDPASSVEMV	KVLEEDPMVG	GVGGDVQILN	KYDSWISFLS	SVRYWMAFNI	266
xlHAS	LDELATVEMV	KVLESNDMYG	AVGGDVRIILN	PYDSFISFMS	SLRYWMAFNV	294
cvHAS	ERAAOSFFRT	VQCVGGPIGA	YKIDIIKEIK	DPWISQRELG	QKCTYGDGDR	311
seHAS	ERAAOSVTGN	ILVCSGPIISV	YRREVVPNI	DRYINOTELG	IPVSIQDGR	262
spHAS	ERAAOSLTGN	ILVCSGPIISV	YRREVIIPNL	ERYKNOTELG	LPVSIQDGR	261
huHAS	ERACOSYFGC	VQCISGPIGM	YRNSVLEHVF	EDWYNQFEMG	NQCSFGDGRH	316
xlHAS	ERACOSYFDC	VSCISGPIGM	YRNNILQVFL	EAWYRQKELG	TYCTLGDRH	344
cvHAS	LITNEILMRGK	KVVFTPPFVG	WSDSTNVFR	YIVQOTRWSK	SWCREIWTYL	361
seHAS	LITNYATDLG	KTVYQSTAKC	ITDVEKDMST	YLKQONRWKN	SFFRESIISV	311
spHAS	LITNYAIDLG	RTVYQSTARC	DTDVEFQFKS	YLKQONRWKN	SFFRESIISV	310
huHAS	LITNRVLSLGY	ATKYTARSKC	LTETPIEYLR	WLNQOTRWSK	SYFREWLINA	366
xlHAS	LITNRVLSMGY	RTKYTHKSRA	FSETEISLYR	WLNQOTRWSK	SYFREWLINA	394
cvHAS	FAAWKHGLSG	ILAFECYLYQ	ITYFFLVIYL	FSRLAVEADP	RAQTATVIVS	411
seHAS	KKIMNPNPVA	LNTILEVSMF	MLLVYSVVD	FVGNVREFDW	LRVLAFLVII	361
spHAS	KKILSNPIVA	LNTIFEVVMF	MLLIVAIGNL	LFNQAIQDL	IKLFAFLSII	360
huHAS	MWFHKHH---	LMVTYEAIT	GFFFFFLIAT	VIQFLYRGKI	WNILLFLTIV	413
xlHAS	QWVHKHH---	LMVTYESVVS	FIFFFFITAT	VIRLIYAGTI	WNVVWLLLCI	441
cvHAS	TTVAIIKCGY	FSFRAKDIRA	FYFV-LITFV	YFFCMIFARI	TAMMLWDIG	460
seHAS	FIVACRNHI	YM--LKHPLS	FLLSPFYGV	HLFVLOELKL	YSLFTIRNAD	409
spHAS	FIVACRNHV	YM--VKHPAS	FLLSPFYGIL	HLFVLOELKL	YSLFTIRNTE	408
huHAS	QLVGIKSS-	FASCLRGNIV	MVFMSSVSVL	YMSLLPAKM	FAIATINKAG	462
xlHAS	QIMSIFKSI-	YACWLRGNFI	MLLMSLSML	YMTGLLESKY	FALLTLNKTC	490
cvHAS	WDIRGGNEKP	SVGTRVALWA	KQYLIAYMW	AAVVGAGVYS	IVHNWMFDWN	510
seHAS	WGT----RKK	L-----	-----	-----	-L*	417
spHAS	WGT----RKK	V-----	-----	-----T	IFK*	419
huHAS	WGTSG--RKT	IVVNFIGL--	---IPVSVMF	TILLGGVIFT	IYKESKRPF	505
xlHAS	WGTSG--RKK	IVGNYPIM--	---LPLSIWA	AVLCGGVGYS	IYMDCCNDWS	533
cvHAS	S-----LSYR	FALVGIC-SY	IVFIVIVLVV	YFTGKITWN	FTKLQKELIE	554
huHAS	ES-QQTVLIV	GTLLYAC---	--YVWMLLT	YV---VLINK	CGRRKKGGQY	546
xlHAS	TPEQKEMY-	-HLLYGCVG	VMYVWIMAVM	YW---VWVKR	CCR-KRSQTV	577
cvHAS	DRVLYDATTN	AQSV*				561
huHAS	DMVL----	DV*				552
xlHAS	TLVH----	DI	PDMCV*			588

FIG. 2

Phylogenetic tree showing the relationships between various HAS domains. The tree is rooted at the bottom with xlHAS. The first major split is between the seHAS/spHAS clade (67.2%) and the rest of the tree. The second major split is between the muHAS2/huHAS2 clade (98.7%) and the muHAS3/muHAS1/huHAS1/xlHAS clade (40.9%). The muHAS2/huHAS2 clade further splits into muHAS2 (58.0%) and huHAS2. The muHAS3/muHAS1/huHAS1/xlHAS clade splits into muHAS3 (46.6%) and a sub-clade containing muHAS1 (94.1%), huHAS1, and xlHAS. The final split in this sub-clade is between muHAS1 (46.6%) and the huHAS1/xlHAS clade.

Domain	Support Value (%)
seHAS	67.2%
spHAS	
muHAS2	98.7%
huHAS2	58.0%
muHAS3	40.9%
muHAS1	94.1%
huHAS1	46.6%
xlHAS	

FIG. 3

SIZE DISTRIBUTION OF HYALURONAN
PRODUCED BY DIFFERENT ENGINEERED
STREPTOCOCCAL HAS ENZYMES

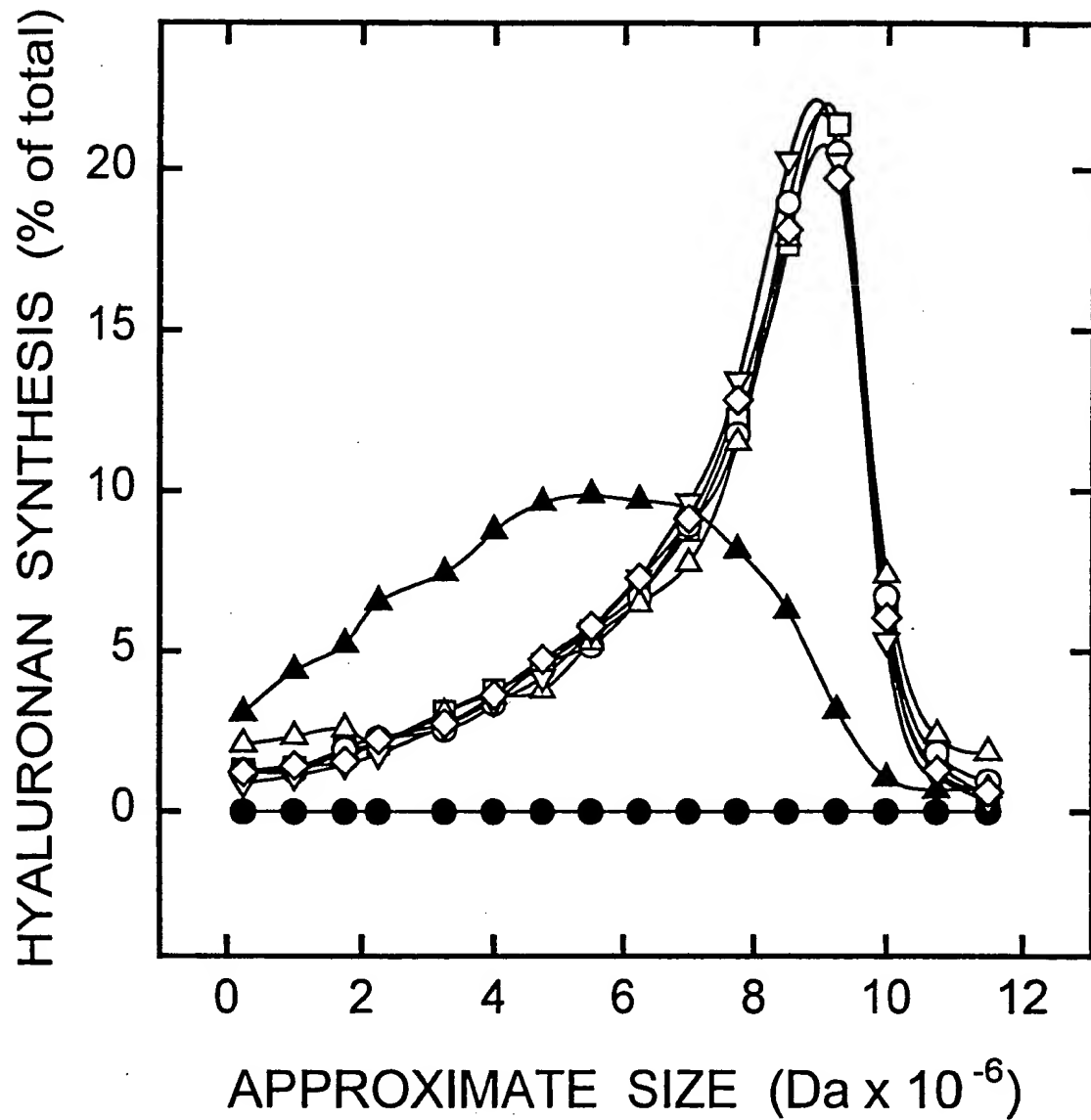


FIG. 4

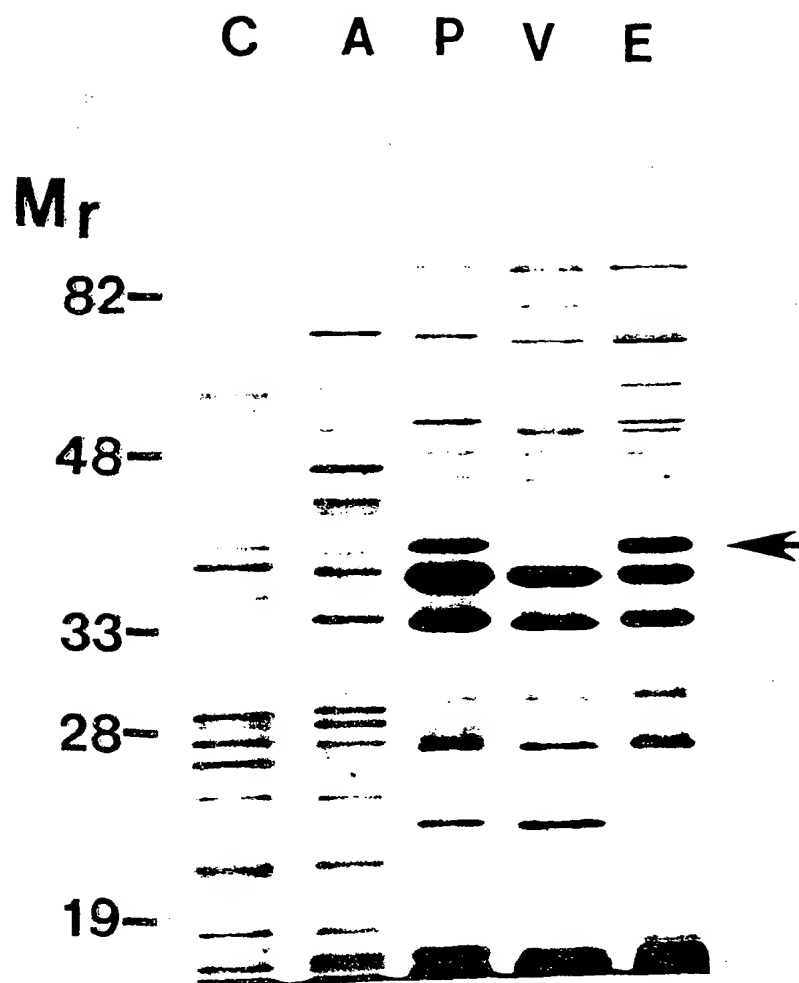


FIG. 5

66T22T 00269460

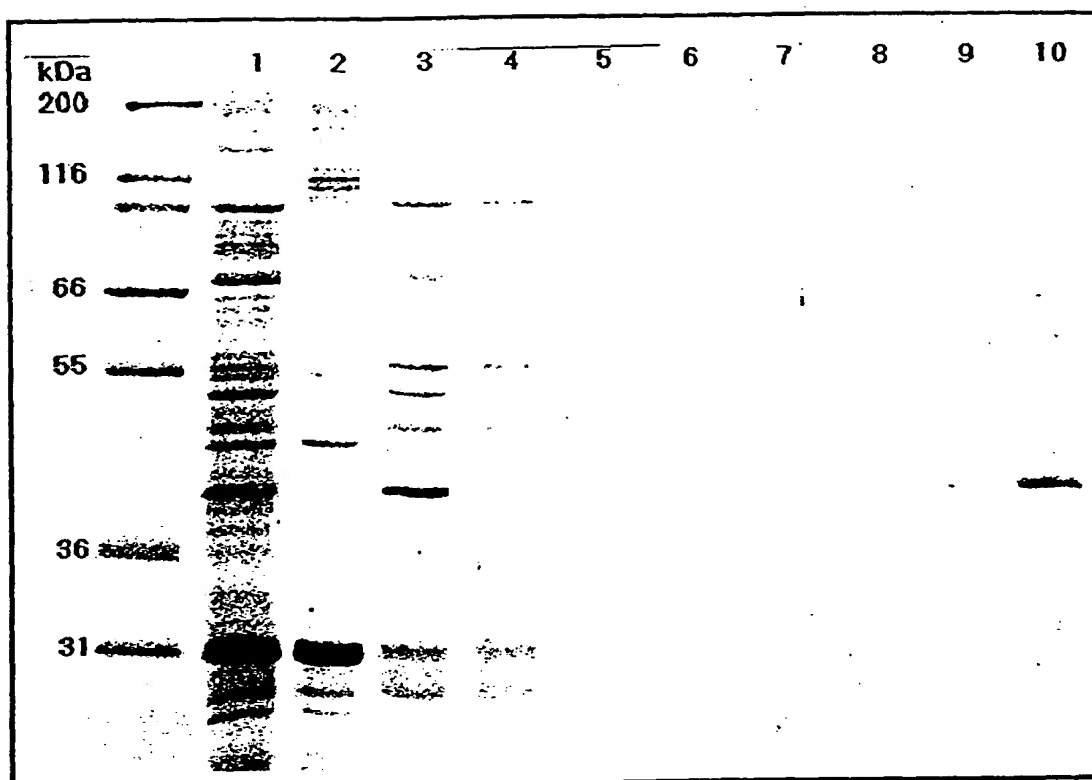


FIG. 6

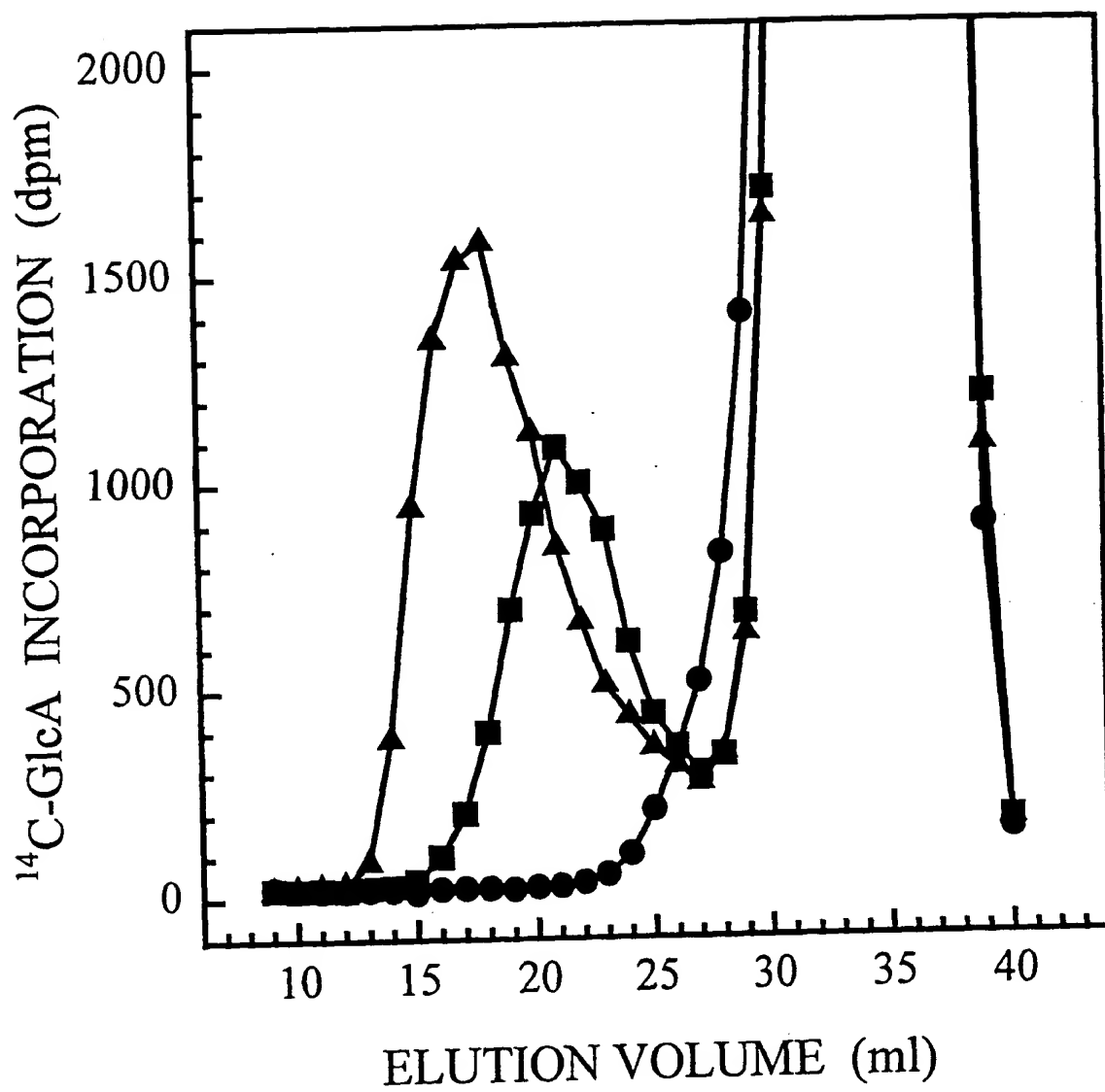


FIG. 7

00469200.12199
661221 00269460

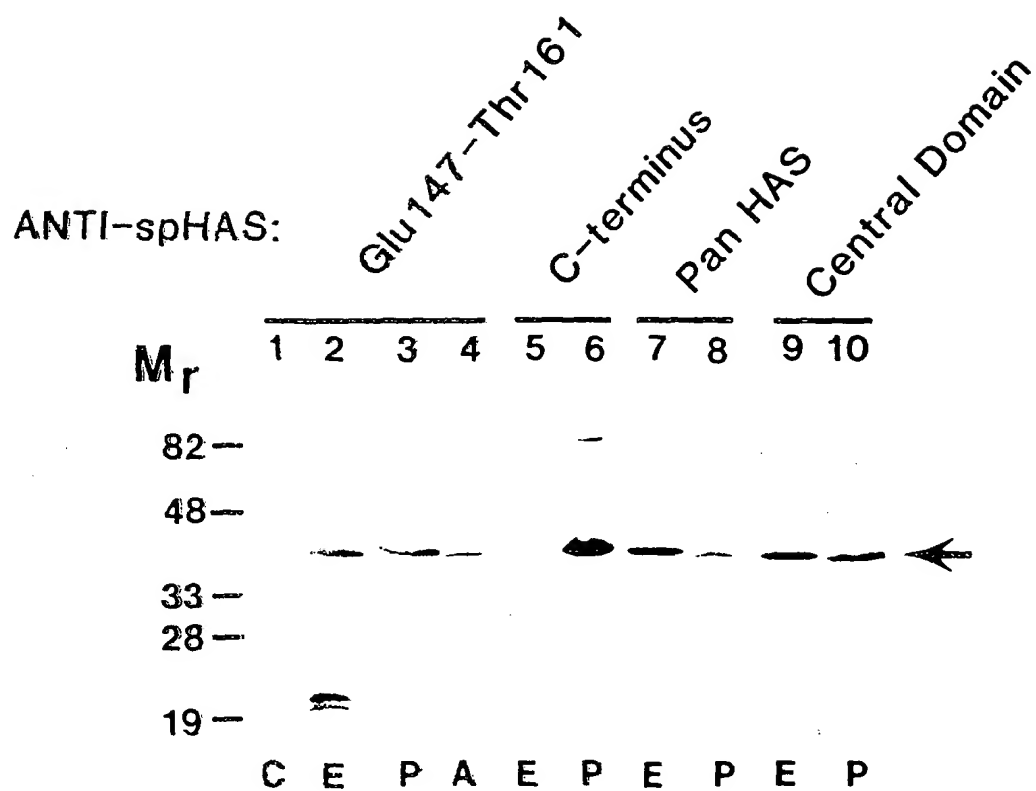


FIG. 8

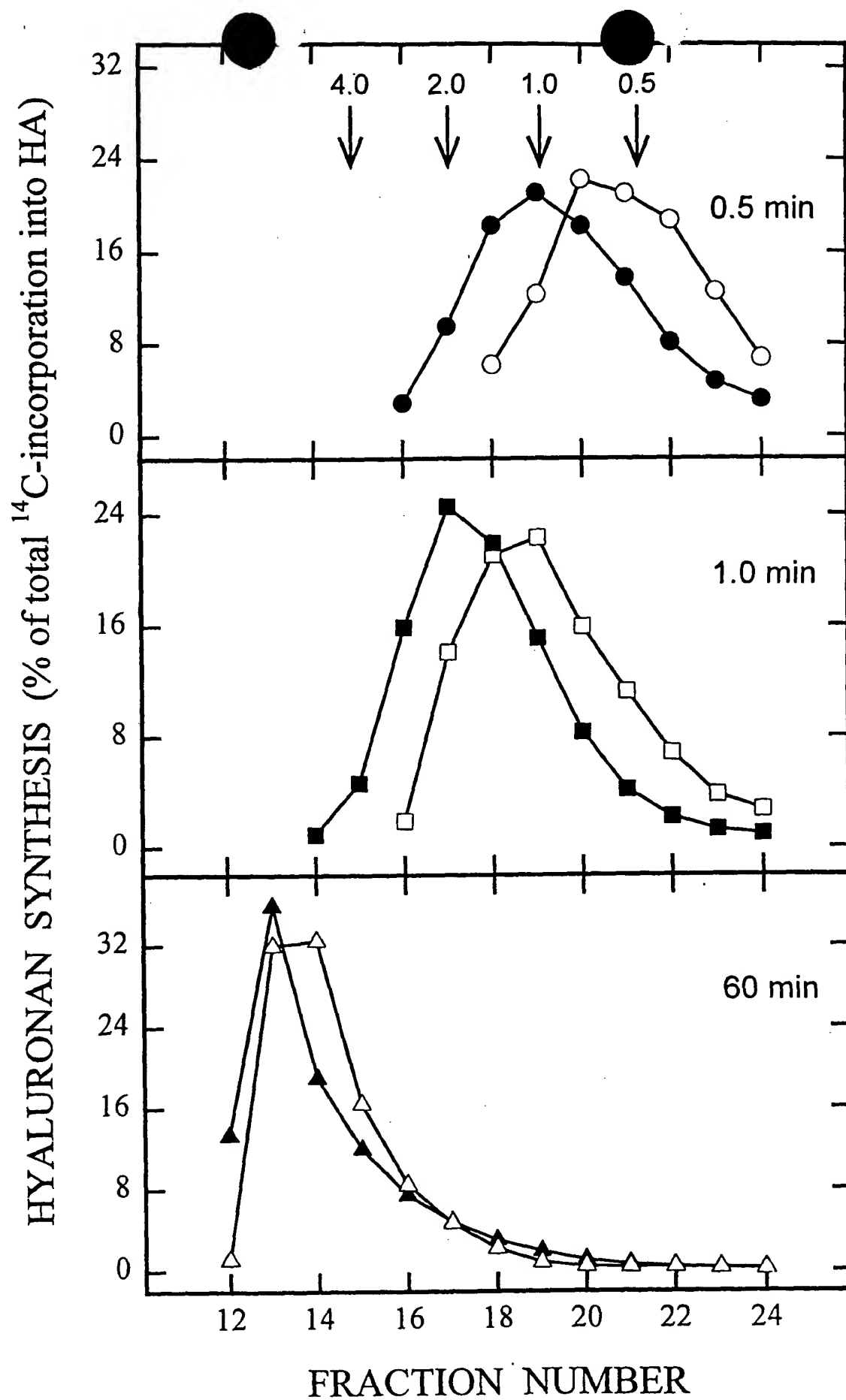


FIG. 9

661227.0025460
HYDROPHILICITY

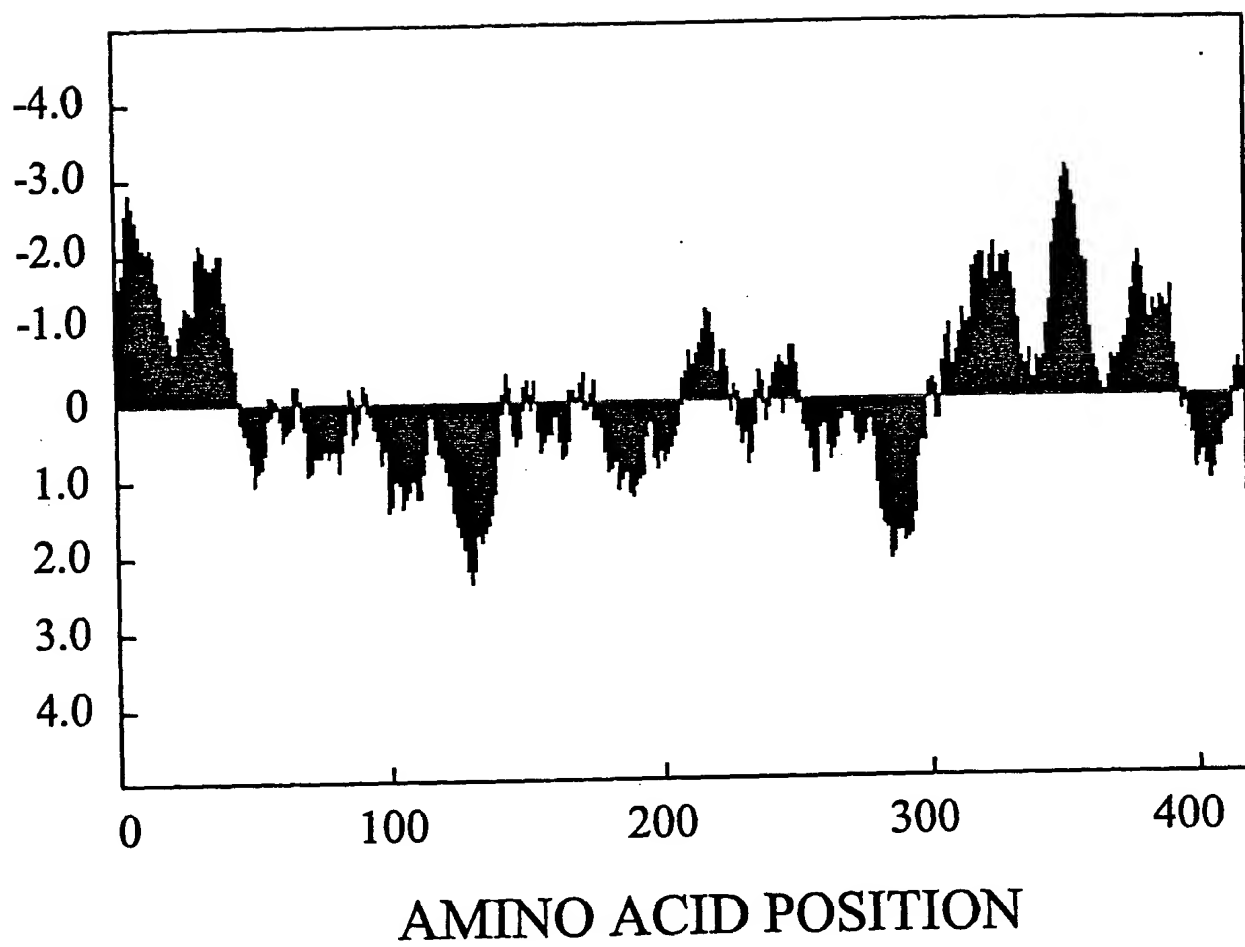


FIG. 10

OUTSIDE

MD1 MD2 MD3 MD4 MD5

INSIDE

NH₂

COOH

C 226 C 262 C 281 C 367

FIG. 11

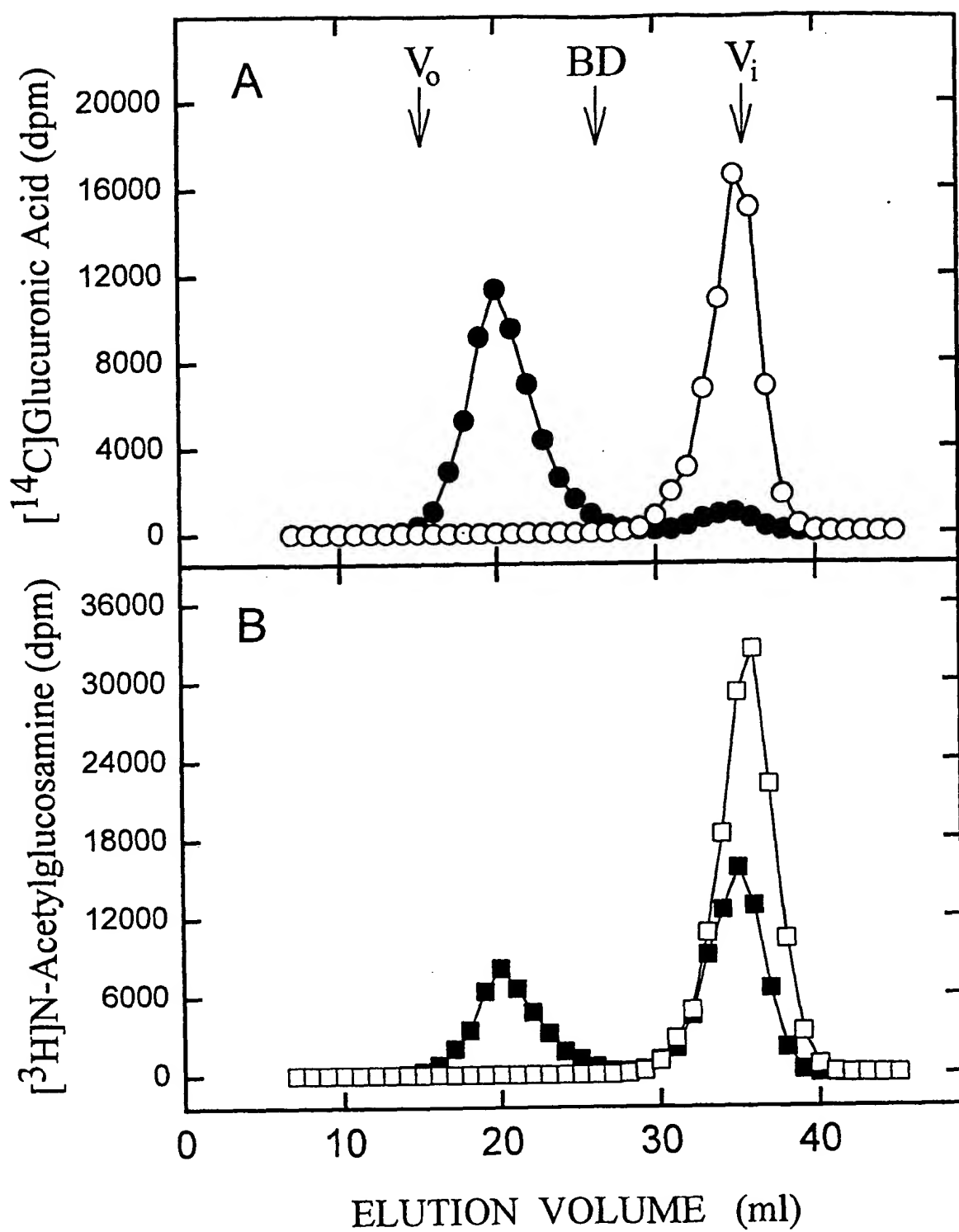


FIG. 12

667227-00259453

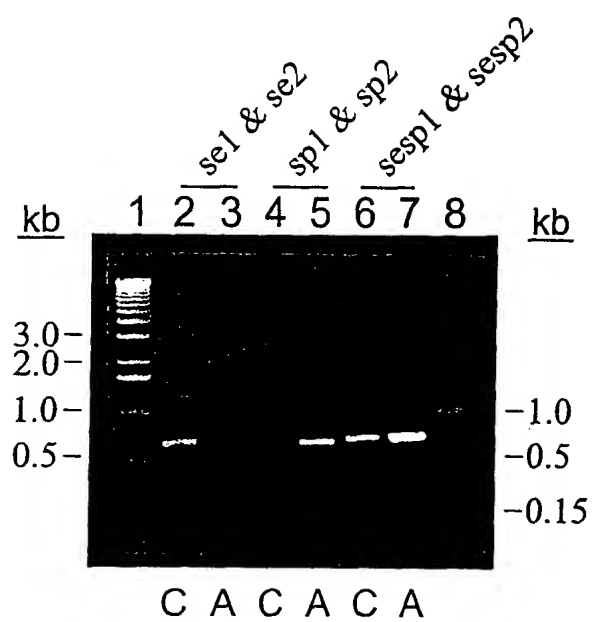


FIG. 13